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Review article

Inhalation device requirements for patients' inhalation maneuvers

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ABSTRACT

Background: Inhaled drugs are the mainstay of treatment for lung diseases such as asthma and chronic obstructive pulmonary disease. However, failure to use inhalation devices correctly can lead to a poorly controlled status. A vast number of inhalation devices exist and each device has specific requirements to achieve optimum inhalation of the drug. Currently, there is no overview of inhalation requirements considering all devices. This article presents a review of the literature on different inhalation device requirements and incorporates the data into a new inhalation flow algorithm.
Methods: Data from literature on commercially available inhalation devices were evaluated and parameters, such as inhalation flow rate, flow acceleration, inhalation volume, and inspiration time assessed for the required inhalation maneuver specific to the device. All agreed upon data points were used to develop an inhalation flow algorithm.
Results: The literature analysis revealed availability of robust data for the required inhalation flow characteristics for most devices and thus for the development of an algorithm. For those devices for which these parameters are not published, the minimum required flow criteria were defined based on published data regarding individual aspects of aerosol quality.
Conclusions: This review provides an overview of inhalation devices available on the market regarding requirements for an acceptable inhalation maneuver and shows which goals should be achieved in terms of inhalation flows. The presented algorithm can be used to develop a new computer based measurement system which could help to test and train patients' individual inhalation maneuvers with their inhalation devices.

Contents

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1. Introduction

Inhalation is the preferred route of drug administration for patients with lung diseases such as asthma and chronic obstructive pulmonary disease (COPD). The development and introduction of the pressurized metered dose inhaler (pMDI) in 1956 provided the first handy, reliable inhalation device [1,2]. In the following period, the device became a worldwide success [2]. The quality of pMDIs has continually improved over time, particularly since the ban on chlorofluorocarbons (CFCs) [2]. With the required changeover to alternative propellants, several products were fundamentally modified, which also led to changes in aerosol quality that were relevant for practice [1–6]. Key achievements since the switch from CFC to HFA (hydrofluoroalkane) are devices with slower exit velocities and warmer plumes [2,3,6]. A reduction in speed, combined with smaller particles for some products, led to significantly improved lung deposition of the active drug particles [1,2,4–6]. Next to pMDIs, dry powder inhalers (DPI) play a significant role in the treatment of diseases such as asthma and COPD. In 1987, the first multidose DPI device with budesonide, an inhaled glucocorticosteroid (ICS), was used [7]. Today, in addition to pMDIs, there are a number of devices available with medications in powder form.

The quality of inhalation devices is generally high and active drug delivery is reliable if the devices are used properly. The key factors for successful inhalation, however, involve the right particle size and a proper respiratory maneuver on the part of the patient [6,8]. Each inhalation device requires a specific preparation for reliable drug delivery. One of the most common sources of errors in the application of pMDIs is the lack of coordination between inhalation and the actuation of the inhaler [6]. With DPIs, inspiratory flow rates that are either to low or lack the necessary initial acceleration compromise treatment success [6]. While the handling of the inhaler, such as preparation (e.g. removing the protective cap and preparing the dose), positioning of the device (e.g. keeping it vertical) and follow-up (such as replacing the protective cap and storing it in a dry place) can be monitored by a therapist observing the inhalation process, there is currently no validated and easily available method in place for monitoring the quality of the complete inhalation maneuver with different devices.

In an editorial entitled “Dry Powder Inhalers and the Risk of Error”, Terzano formulated the following questions and requirements regarding the necessary inhalation energy in the application of breath-actuated DPIs: “The issue of flow independence makes it imperative to determine two parameters for all breath-actuated DPIs: Below which flow rate does the DPI performance fall dramatically? Above which flow rate does the DPI performance become fairly stable?” [9] Similarly, Laube et al. pointed out in their task force report that “no manufacturer has stated the minimum flow for their DPI, although it is clear that this information is needed.” [6].

An overview of such flow limits for all inhalation devices on the market is still lacking. However, these data are necessary to assess the quality of an individual inhalation maneuver. For the development of a new computer-assisted measurement system that can be used to measure and assess multiple aspects of the inhalation maneuver with original devices including inspiratory flow rate, inhalation time, acceleration rate, and inhalation volume, it was necessary to determine a measuring algorithm based on known and published data regarding flow value limits of inhaler requirements and inhalation quality.

2. Materials and methods

A literature search was conducted for publications released between 1980 and 2015 with the aim of determining all dependencies of inhaler performance on inhalation flow rate and inhalation maneuvers. The year 1980 was chosen to ensure that we included and discussed all relevant data on optimum inhalation flow rates for modern DPIs which were first launched in 1987. No years prior to 1980 were reviewed, as they could not include data on HFA-MDIs. Search terms included “inspiratory flow”, “inhalation maneuver”, “inhalation technique”, “inhalation volume”, “flow acceleration”, “drug delivery”, “inhalation device”, and specific product names. Furthermore, parameters that are important for good inhalation results with commercially available inhalation devices, including pMDIs, DPIs, and breath-actuated inhalers (BAIs) were searched for including the following: minimum required inspiratory flow rates (bottom limit of the flow rate), optimum inspiratory flow rates, maximum inspiratory flow rates (upper limit of the inspiratory flow rates), flow acceleration, inspiration time, as well as inhaled volume after release or achievement of the minimum required inspiratory flow. The results of the search were complemented by literature cited in review articles. Publications were considered for review if they provided clear product specific information regarding effects of various flow parameters (e. g. flow rate) on clinical outcome and/or on aerosol quality criteria such as output, mass median aerodynamic diameter (MMAD), fine particle dose (FPD) and fine particle fraction (FPF). If publications did not meet these criteria they were excluded, no other exclusion criteria were used. Existing systematic reviews were included in this review. Next to full published articles and reviews in English, German text books and publications as well as editorials, instructions for use, poster abstracts, summary of product characteristics, the United States Pharmacopoeia, assessments of the European Medicines Agency (EMA) as well as other materials that were considered to be important to the topic were included in this review.

Data for inhalation flow rates and – if deemed necessary–other inhalation parameters are presented and discussed for individual inhalers. All agreed upon data points were then used to develop a new algorithm which could be used to measure and interpret quality of the inhalation maneuver with different inhalation devices.